

D. F. Payne with W. Hale White

Kind regards

on Case of Hypnotical Pyrexia with
Literature of subject - see Clin Trans
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on remarkable cases of Pyrexia see
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THE NEUROTIC THEORY OF PYREXIA.

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NOT very long ago the cause of the rise of temperature in febrile disturbances was unknown. Now, however, it is pretty universally allowed to be due to altered chemical changes going on in the thermogenetic tissues of the body. Whether this alteration be a cessation of chemical processes in which heat is normally used up, as has been ingeniously suggested by Dr. Ord in the *British Medical Journal* for October 25th, 1885, or whether they are destructive chemical changes setting free heat, does not concern us in the subject of this paper. But that there is an alteration is shown by the great increase of urea, considering the diet, during fever, and also by the great increase of the salts of potash in the urine and the diminution of those of soda, this fact showing that the changes go on in the muscles or blood corpuscles, and not in the plasma; the amount of carbonic acid gas is also allowed to be augmented, but results not quite so exact as those in respect to the urine can be obtained on this point. Then again the wasting of the muscles, which are the chief thermogenetic tissues of the body, is roughly proportional to the amount of fever. Patients

take longer to recover their robust health after typhoid than after any other fever, and in this disease one generally finds the muscles of the extremities more wasted than in any other, this being due to the fact that it is in typhoid that the febrile condition lasts longer than in most diseases. In connexion with this it is interesting to note that it is in typhoid that one generally finds degeneration of muscle. Should any one urge that the muscular wasting and increased excretion of urea do not go invariably hand in hand with the rise of temperature, he need only be reminded that the thermometer is not an accurate gauge of the increased production of heat, for the temperature as registered by the thermometer indicates the increased production, minus the increased loss from evaporation, radiation, and conduction. The increased production of heat for its exact determination requires calorimetrical experiments, the difficulties of which are so great that any results obtained from the human subject are valueless. No doubt defective assimilation has also something to do with the wasting in fever, but still it will be admitted that the wasting of the muscles is proportional roughly to the amount of fever. This shows clearly that in fever, at least, the muscle has a thermogenetic function apart from its motor one. Likewise during health muscles are the organs for the production of movement and also for the production of heat. Now in connexion with this there are two possibilities, either that the chemical changes which are the means of the conversion of potential energy into the two forms of mechanical motion and heat (kinetic energy) are the same, and that some unknown cause determines into which the potential energy shall be converted, or that there are two series of chemical changes going on side by side, as in the liver for example, and the result of one is heat and the result of the other is motion. Of course when a muscle contracts it becomes slightly warmer, but that increase is too slight to render it likely that the few muscular movements performed during sleep can keep the temperature up to normal. Perhaps it is more a question for a physiologist than a physician whether or not the muscles have two functions, but certainly seeing that during increased motion there is no increase of urea, whilst during increased heat production there is, it seems probable that the muscles have two distinct functions, each of which is

accompanied by different chemical changes. As further proof that the motor function is separate from the thermogenetic function there are the numerous cases of cerebral hæmorrhage causing hemiplegia, in which, in spite of the loss of motion, there is an elevation of temperature. Bourneville¹ has recorded several of these ; some more will be found recorded by me in the *Guy's Hospital Reports*, vol. xlii.² and in the *Lancet*.³

In the article in the *Guy's Hospital Reports*, already referred to, I showed that there was very strong evidence to prove that the central nervous system presided over the heat-production of the body, and that therefore the bodily temperature might deviate from the normal in cases of injury or disease of the nervous system ; and the object of this short paper is to examine how far we are justified in looking upon febrile pyrexia as a symptom of a disorder of the nervous system acting upon the metabolism of the muscular tissues. I therefore begin by giving the reasons for supposing that the muscles do produce the pyrexia of fever.

So far from it seeming strange that nervous action should manifest itself in heat, it would rather be extraordinary if it did not do so sometimes, for, after all, nervous action is merely a manifestation of energy, and is therefore, like electricity, capable of conversion into other forms, such as motion and heat.

The diagram on page 4 will, I think, represent the parts of the nervous system which are capable of affecting the temperature of the body apart from vaso-motor fibres.

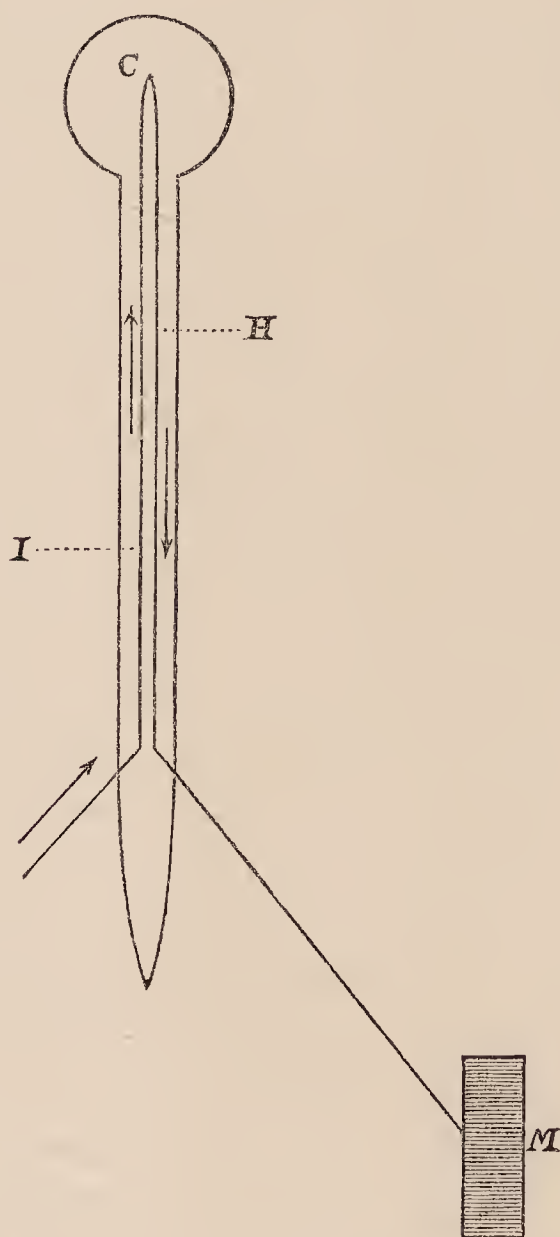
Let us now see whether the nervous system of calorific nerves can be held responsible for the pyrexia of ordinary fever. Before doing this it will be necessary to put aside the vaso-motor system. To produce pyrexia this can only act either by causing contraction of the cutaneous vessels, and thus impairing the loss of heat, or by dilating the muscular vessels and therefore aiding the production. In the beginning of this paper the reasons for believing fever to be due to increased production and not to decreased loss of heat were given, so that the first possible mode of vaso-motor action can be put out of count. Whether the

¹ Bourneville, *Études cliniques et thermométriques sur les Maladies du Système nerveux*.

² "The Theory of a Heat Centre from a Clinical Point of View," *Guy's Hosp. Rep.* vol. xlii. series iii.

³ "A Case of Neurotic Pyrexia," *Lancet*, July 25, 1885.

altered tissue change that goes on in muscle is due to the fact that more blood is brought to the muscle owing to some special muscular vaso-motor change, or whether the change is due to genuine calorific nerves ending in the muscle, is a question very



C. Inhibitory centre in the brain, probably near the fissure of Rolando, which exercises a restraining influence on the thermogenesis of the body. H. Fibres proceeding down the cord to the muscles, and conveying the restraining influences from the centre C. I. Fibres ascending to the brain centre, which is capable of being affected by their stimulation. M. Muscle, the thermogenetic tissue.

difficult to decide. The probability is that the cerebral centre is not muscular vaso-motor, but a genuine calorific one, for stimulation of a nerve going to a part will cause a rise of temperature even if the blood supply be cut off. Also Wood¹

¹ H. C. Wood, "Fever," *Smithsonian Contributions to Knowledge*, 357, Philadelphia, 1880.

has found that in an animal in which the vagus and splanchnics are divided, stimulation of a sensory nerve, by acting on the small vessels whose sympathetic was not destroyed (*i.e.* chiefly muscular ones), caused a rise of blood pressure, and destruction of the supposed calorific centre near the fissure of Rolando did not affect the pressure in either way, therefore it is concluded that the centre is not a vaso-motor one. In another experiment he found that after separation of the pons and medulla, and division of the splanchnics and vagi, blood-pressure still rises on stimulation of a sensory nerve, from which he concluded that the muscular vaso-motor centre exists below the junction of the pons and medulla. Lastly there is no evidence that antipyretic drugs, such as quinine or kairin, contract muscular vessels.

Thus we see it is improbable that the calorific centre is a muscular vaso-motor one, and that therefore if the nervous system is to be credited with any share in the raising of the temperature in fever it is by a direct thermogenetic action.

All cases of pyrexia fall into one of four classes. Firstly, those in which the rise of temperature is due to a zymotic disease; secondly, those in which it is due to inflammation; and thirdly, those such as traumatic fever in simple fracture, and urethral fever, in which the cause is obscure; fourthly, those in which it is due to injury or disease of the nervous system, as in the cases in which the temperature goes up in fracture of the spine, cerebral hæmorrhage, &c.

In the first class the universal characteristic is the presence, either real or hypothetical, of some special living poison. Now this living poison may either act directly on some part of the thermogenetic apparatus, or it may manufacture some substance which acts as a poison. Which of these views is the true one does not matter as far as we are now concerned; we know that in septic poisoning the poisonous material is manufactured at the seat of inoculation by the septic bacteria, whilst in other cases, such as relapsing fever, the micro-organisms circulate in the blood, but even then it may be something they produce, and not they themselves, which cause the pyrexia.

It is just possible it might be urged that in those zymotic diseases in which there is a local inflammation, the chemical changes going on there are the cause of the pyrexia; this

has only to be mentioned in order to be refuted, for there is no correspondence between the amount of local trouble and pyrexia in, for example, typhoid fever, and if in this disease the rise of temperature were due to changes in the intestine, it would be difficult to explain all the facts which have been brought forward to prove that in fever it is the muscular changes which are the cause of the pyrexia. The problem now is to decide, whether in zymotic disease the poison produced by the micro-organisms (or in some cases perhaps the micro-organisms themselves), act on the muscles directly to increase their thermogenesis, or indirectly by cutting off the inhibiting influence of the cerebral calorific centre either by acting directly on that centre or on the nerve fibres from it to the muscle, or on the termination of the nerve fibres in the muscle, or lastly whether it acts upon the afferent nerves (or their peripheral terminations) proceeding to the calorific centre. I am not aware that any experimental work has been done to settle this question. The experiments would be very difficult to carry out, and still more difficult of interpretation. In order to ascertain whether the poison acted on the cerebral centre one might destroy it, whereupon the temperature would rise, the restraining influence on muscular thermogenesis being cut off; if now the injection of septic material produced no pyrexia it might be urged that the poison acted upon the cerebral centre. It is, however, a waste of time to devise experiments unless one is able to perform them. The weak part of the theory, which supposes that in the fever due to zymotic disease the poison stimulates either the cerebral centre, the nerves proceeding from it, or the terminations of the nerves in the muscles, seems to me to be that the centre and the nerves proceeding from it are inhibitory to the thermogenesis, and therefore their stimulation ought to mean a fall of temperature, just as stimulation of the cardio-inhibitory centre means a diminution in frequency of the cardiac beats. It is true that the zymotic poisons might all act as depressants of the restraining system of nerves, in which case the temperature would rise, but it certainly seems more natural to suppose that they would stimulate it. But supposing the poison acts neither as a depressant on the inhibiting calorific nervous mechanism, nor as a direct stimulant

to the thermogenesis in the muscles, there is still the possibility that the centre may be affected through the influence of an afferent nerve.

In physiology there are many examples of this reflex action through an afferent nerve acting on a cerebral centre. Thus stimulation of the sciatic nerve will produce glycosuria, by its action on the hepatic vaso-motor or diabetic centre in the medulla. In this case the stimulus proceeding by means of the sciatic to the medulla has the effect of taking off the restraining influence which the diabetic centre continually maintains upon the hepatic artery, and thus the branches of it in the liver dilate and glycosuria results. With this fact before us we might expect that stimulation of the sciatic nerve by its effect upon the cerebral calorific centre might diminish its restraining power, and thus cause a rise of temperature. The earlier experiments seemed to show that this peripheral stimulation might cause a rise of temperature, but lately it has been maintained that if the movements of the animal be done away with by means of curare then stimulation of a peripheral nerve causes a fall of temperature. But these experiments of Heidenhain's¹ are certainly not applicable to man. Naumann² tried to confirm them, and stated that stimulation of the skin by liquor epispasticus caused a general fall of temperature, but Jacobson³ in a short article, in which he recounts some experiments he made in Prof. Frerich's clinique in Berlin, shows that neither with stimulation by blistering fluid nor stimulation by electricity does one, if the experiments be properly performed, get a fall of temperature—in fact in the majority of his experiments he got a rise, and even when there was a fall it was so slight as to be hardly noteworthy. He concludes that the cause of the different results obtained by himself and Naumann was that the latter performed his experiments carelessly, not taking proper means to record the temperature accurately. He does not see any chance of reconciling the results on the supposition that the stimuli were of different strengths in the two sets of experiments. Heidenhain made a great point of the fact that

¹ Heidenhain, *Pflüger's Archiv für Physiologie*, 1870, 1871, 1872.

² Naumann, *Vierteljahrsschrift für die practische Heilkunde*, Bd. 93.

³ Jacobson, *Virchow's Archiv*, Bd. 67.

when he had induced fever in animals stimulation of a nerve no longer caused a fall of temperature; but in the article just referred to Jacobson has shown that this does not apply to man, because in the great majority of fever patients to whom he applied peripheral stimulation to the nerves he got no fall of temperature, but a rise. He does not allude to it, but is it not just possible that the fact that Heidenhain's animals were poisoned with curare, may have had something to do with the results he obtained; for we know that it poisons motorial end plates, and the calorific fibres from their commencement near the fissure of Rolando, to their termination in muscles, run so near to the motor that it is hardly an exaggerated supposition to suppose that they may be affected by curare. But whatever may be the cause of the discrepancy between Heidenhain's experiments on animals, and Jacobson's on man, we can hardly, I think, with regard to fever in man, agree with Redard¹ who concludes his discussion on the subject by saying that excitation of sensory nerves and pain lower the temperature in the majority of cases. Jacobson's experiments are too important to permit this conclusion. Thus we see that it is quite possible to assume that zymotic pyrexia may be caused by a poison circulating in the blood, which poison, acting on the periphery of afferent nerves, causes impulses to be conveyed to the calorific cerebral centre, which have the effect of diminishing the restraining influence it perpetually exercises on the thermogenesis of the body.

Let us now consider the pyrexia due to inflammatory processes. The most important fact to bear in mind here, is that the size of the inflamed part bears little or no relation to the height of the temperature. Thus the temperature is often higher with an abscess of the tonsil than in much more extensive inflammations. Now it might be put forward, as an explanation of pyrexia, that it was due to some poison manufactured at the seat of inflammation, and that this circulating through the body acted either upon the muscles, the thermogenetic centre, the efferent nerve connecting these or on some afferent nerve affecting the centre; but the fact that the amount of pyrexia bears no relation to the size of the inflamed part is against this hypothesis, for the

¹ P. Redard, *Traité de Thermometrie médicale*.

amount of poison manufactured would bear some relation to the amount of inflammation, and the pyrexia again would vary directly with the amount of the poison. If one calls to mind all the cases one has come across in which there has been considerable pyrexia without a large inflammatory area, it will, I think, be allowed that the only common characteristic of these cases is that in all of them there has been a considerable tension of parts, the pus having been tightly bound down; furthermore, in all the cases in which the temperature is not so high as one would expect considering the amount of inflammation, one finds that the pus is not tightly bound down; thus it is very remarkable that with such a large area involved the temperature should not be higher than it is in empyema, peritonitis, and meningitis, but it will be noticed that of all inflammations these are just the ones in which, from the very nature of the parts, the pus is not tightly bound down. Statistics would be of little service in determining this point, for the cases vary so in other details that they are hardly capable of comparison. Then again, with regard to the tenseness of the part containing the pus, it is noteworthy how, when there is a quantity of pus causing much tension, the temperature falls directly the abscess is opened.

Ever since the thermometer came into use it has been a common observation that the more acute the inflammation the higher the temperature; thus a cold abscess containing large quantities of pus will not send up the temperature nearly so much as an acute tonsillitis, which even may not go on to the formation of pus; but the great distinguishing feature between the two groups of cases is that in the latter the tension is so much greater than in the former, for the pus in them is so slowly formed, that it does not exert much tension on the surrounding parts.

No one will maintain that in the case of a small inflamed area, such as a tonsil, a temperature of 105° F., which is often reached in these cases, can be due to the chemical thermogenetic changes in the tonsil; if not so, it is only natural to suppose that they go on in the normal thermogenetic tissues, the muscles. If so, although there is the possibility that some substance formed at the seat of inflammation may be carried to the muscles and set up increased thermogenesis there, it seems to me more probable, inasmuch as the extent of the inflamed area bears no

relation to the temperature, but the tension of the inflamed parts does, that the cerebral calorific centres are affected reflexly by the tension of the inflamed part acting as a stimulus which takes off their normal inhibition just as other cerebral centres may be affected reflexly. If it be urged that in cases of cysts, hydrocephalus, &c., there is often great tension without any rise of temperature, it must be remembered that in these examples the tension is very slowly developed, and that as a rule the effect of a stimulus slowly applied to a nerve is different from the effect of one applied rapidly; furthermore, in fever, in addition to the tension, there may be some other factor such as damage to the nerve terminations by the inflammatory products.

We now come to the third group of cases in which the pyrexia is not due to either a zymotic disease, inflammation, or obvious affection of the nervous system. As examples of such we may take traumatic fever and urethral fever. They need not detain us long, for they are exactly comparable to the second group, being in all probability reflex, the stimulus being applied at the point of injury. They were fully treated by Mr. Victor Horsley in his Brown Lectures last year, and he points out how the cases in which there is swelling may be explained by supposing that tension is the exciting cause. In those cases in which there is no swelling, it may be that some poison is developed at the point of injury, and that it, acting as a stimulus to the peripheral termination of the afferent nerve of the calorific centre, sets up the fever; or again, the stimulus may be the actual laceration of the afferent nerve fibres; or lastly, there may be severe swelling and consequent tension resulting from the injury, and this may be located in the sheath of the nerve, or in close proximity to it, and therefore not visible externally. Seeing how conveniently the tension theory has in our second group explained fever, perhaps it is not unlikely that here also it may in reality be the genuine explanation. Anyhow, the cases of traumatic fever with no visible swelling emphasise that the rise of temperature is far from directly proportional to the area of the injured tissue, be it inflammatory or not. Therefore, the chemical changes going on at the seat of injury cannot be the cause of the pyrexia, and it is improbable that a poison generated at the seat of injury and carried to the thermogenetic tissues is the

cause, for the quantity of poison manufactured would bear some relation to the area of the poison-producing tissue.

With regard to urethral fever, little is at present known as to its pathology, but considering the suddenness of the onset, which can always be directly connected with the passage of the catheter, there can be but little doubt but that in some way urethral fever is due to nervous influence.

The last group of cases which we have to consider is the very interesting class in which the rise of temperature is due to lesion of the nervous system. Here it is so obvious that the pyrexia is neurotic, that it would be beyond the scope of the present communication to go into much detail about them.

Some of the best recorded instances are to be found in Bourneville's treatise on the subject. Bastian has recorded some interesting examples in the *Clinical Society's Transactions*, and I have collected together some twenty cases in which, with a nervous lesion, the temperature deviated from the normal, and have shown that a careful consideration of these cases points to the conclusion that the thermic centres are in the neighbourhood of the fissure of Rolando, and that thermic fibres descend to the muscles by following much the same course as the motor fibres.

The theory of pyrexia here put forward, then, is that in specific fevers, inflammations, traumatic and urethral fevers, the rise of temperature is due to peripheral stimulation of afferent nerves reflexly affecting the calorific centre.

